Skeletal Muscle Circulation

Skeletal Muscle Blood Flow:

- Skeletal muscle constitute 40–45% of body weight, more than any other single body organ.
- At rest, about 15% of the **C**ardiac **O**utput (CO) goes to skeletal muscle. While during strenuous exercise, skeletal muscle may receive up to 70–80% of the CO.
- During rest, blood flow to skeletal muscle average 3–4 ml/min/100gm of muscle. During extreme exercise, this blood flow can increase 25–50 fold, rising to 100–200 ml/min/100gm of muscle.
- During rest, only 10–20% of the muscle capillaries are open, this sufficient to meet the basal metabolic needs of resting muscle. During strenuous exercise, all the capillaries open up.

	Rest	**Exercise**
Cardiac Output	15 %	70 – 80 %
Blood Flow	3 – 4 ml/min/100gm	100 – 200 ml/min/100gm
Capillaries	10 – 20%	All are open

Control of Skeletal Muscle Blood Flow:

1) <u>Nervous regulation</u>:

a) *Sympathetic nor-adrenergic fibers*:

- These are sympathetic vasoconstrictor nerve fibers secrete nor-epinephrine at their nerve endings.
- They act on (alpha) α_1-receptors to produce **V**aso**C**onstriction (VC).
- These fibers have a tonic discharge causing increased resistance of muscle arterioles (= VC) to divert blood to the other organs.
- This VC is of physiologic importance during hemorrhage and circulatory shock or other types of stress.
- The tonic activity of sympathetic nerves is greatly influenced by reflexes from baroreceptors. An increase in **A**rterial **B**lood **P**ressure (ABP) is sensed by the baroreceptors, which causes inhibition of the sympathetic VC activity resulting in dilatation of vascular bed of the muscles as a way to reduce the elevated blood pressure.

- This tonic activity is also regulated by impulses from chemoreceptors, which stimulated by drop in blood pressure. Stimulation of these receptors increases the sympathetic VC activity aiming at elevation of the blood pressure.

b) *Sympathetic cholinergic fibers*:

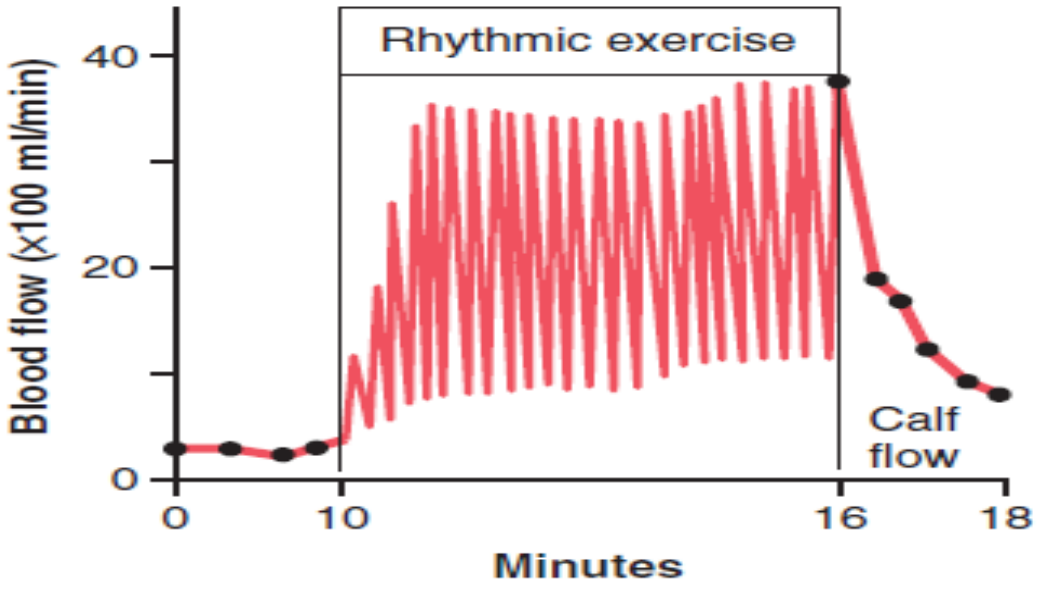
- These are sympathetic vasodilator nerve fibers secrete acetyl choline at their nerve endings.
- They act on (Muscarinic) M_3-receptors to produce **V**aso**D**ilatation (VD).
- They are responsible for the increase blood flow in skeletal muscle <u>at the start</u> of muscular activity (they are activated in anticipation to muscular exercise).

2) <u>Hormonal regulation</u>:

- The medullae of the two adrenal glands also secrete large amounts of nor-epinephrine plus even more epinephrine into the circulating blood <u>during strenuous exercise</u>.
- The circulating nor-epinephrine acts on the muscle vessels to cause a vasoconstrictor effect similar to that caused by direct sympathetic nerve stimulation.
- The epinephrine has a vasodilator effect because it excites more of the (beta) β_2-adrenergic receptors of the vessels, which are vasodilator receptors, in contrast to the (alpha) α_1-vasoconstrictor receptors excited especially by nor-epinephrine.

3) <u>Mechanical regulation</u>:

- The skeletal muscle blood flow is intermittent during muscle contraction. The flow decreases during contraction phase due to compression of the blood vessels by the contracted muscle. Then, the blood flow increases between contractions.



Effects of muscle exercise on blood flow in the calf of a leg during strong rhythmical contraction; the blood flow was much less during contractions than between contractions.

4) <u>Local (chemical) regulation</u>:

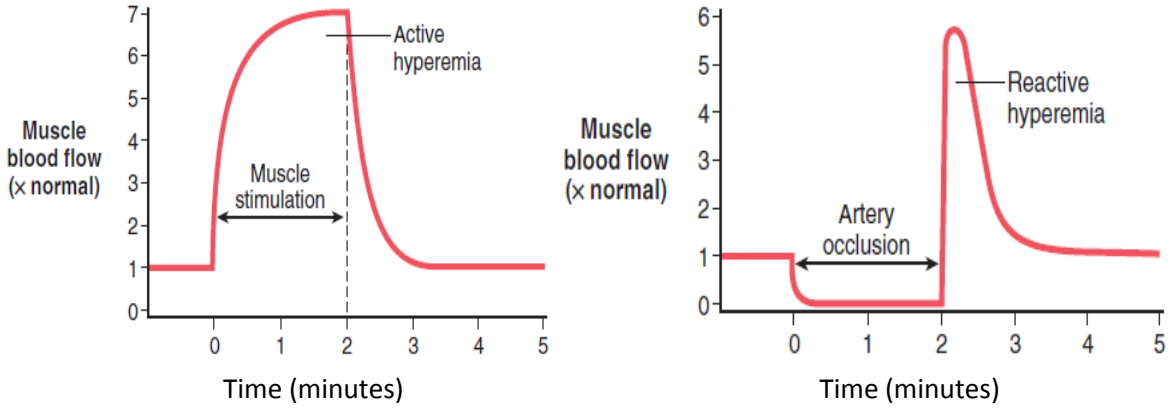
- During exercise, local metabolic factors take over blood flow regulation, regardless of the degree of sympathetic nerve activity. So, when skeletal muscle is active, neural influences on blood flow are overridden by powerful local metabolic control mechanism.
- When muscle contracts, it consumes **O**xygen (O_2) and produce Carbon dioxide (CO_2).
- *Decreased O_2 in muscle greatly enhances blood flow*.
- The reduction of O_2 (low PO_2) causes VD of skeletal muscle blood vessels either <u>directly</u> **or** through <u>release of VD substances</u> (mainly adenosine).
- Vasodilator substances released during muscular contraction include: (1) potassium ions (K^+), (2) **A**denosine **T**ri-**P**hosphate (ATP), (3) lactic acid (H^+), and (4) carbon dioxide.
- The rise of temperature in active muscle constitutes another factor that further dilates the vessels.
- The increased skeletal muscle blood flow due to accumulation of vasodilator metabolites is accomplished by 2 ways:

a) *Active hyperemia*:

- Occurs when tissue metabolic rate increases.
- The increase in local metabolism causes the release large quantities of vasodilator substances.

b) *Reactive hyperemia*:

- Occurs after the tissue blood supply is blocked for a short time.



(a): *Active Hyperemia;* following increased tissue metabolic activity.
(b): *Reactive Hyperemia;* after temporary occlusion of the artery supplying blood flow.

Circulatory Response to Exercise

I) Systemic Circulatory Changes:

A) Increased cardiac output:

- The cardiac output often increase up to 4–5 times normal in the non-athlete, or to 6–7 times normal in the well-trained athlete, to satisfy the metabolic needs of the exercising muscles.
- It is increased during isotonic exercise to values that may exceed 35 L/min (7 times normal) in marathon runners.
- Cardiac output is the product of heart rate & stroke volume. Therefore, increased cardiac output is achieved by increasing both the heart rate & stroke volume

Cardiac **O**ut**P**ut (COP) = **H**eart **R**ate (HR) X **S**troke **V**olume (SV)

Cardiac Output	L/min
Adult male **at rest**	5
Maximum COP during **exercise in un-trained** male	23
Maximum COP during exercise in male **marathon runner**	35

1- *Increased heart rate (HR)*:

- Heart rate is an essential parameter in increasing cardiac output during exercise.
- Heart rate increases during exercise up to rates as high as 170–190 beats/min. It results almost entirely from sympathetic stimulation, plus other minor factors.
- The heart rate is increased as a result of multiple factors including:

a) Emotional (psychic stimuli):
   - These are Stimuli from cerebral cortex to the medullary cardiac centers.
   - It is maximal just before the start of exercise.

b) Decreased vagal tone on the heart:
   - It has a –ve chronotropic effect (= decreasing heart rate, acting on M_2-receptors).

c) Increased sympathetic activity on the heart:
   - It has a +ve chronotropic effect (= increasing heart rate, acting on β_1-receptors).

d) Circulating catecholamines:
   - Secreted from adrenal medulla (mainly adrenaline & lesser amount of nor-adrenaline).

- They have a +ve chronotropic effect (= increasing heart rate, acting on β_1-receptors).

e) Increased body temperature and local temperature of SA node:
- Increased temperature has a direct stimulatory effect on SA node, increasing its rate of discharge and subsequently the heart rate.

f) Increased venous return:
- Increased **V**enous **R**eturn (VR) causing local mechanical stretch of SA node $\rightarrow$ stimulation $\rightarrow$ increasing its rate of discharge and subsequently the heart rate.

g) Impulses from receptors located in active muscles, joints and tendons:
- These receptors are called "porpioceptors".
- They send impulses to activate cardiac centers in medulla oblongata.

h) Impulses from chemoreceptors:
- These receptors are of 2 types: central & peripheral.
- They are stimulated in response to hypoxia ($\downarrow PO_2$), hypercapnia ($\uparrow PCO_2$) and acidosis ($\uparrow H^+$).
- They send impulses to activate cardiac centers in medulla oblongata.

2- <u>*Increased stroke volume (SV)*</u>:
- The stroke volume is increased as a result of enhanced ventricular contraction.
- **E**jection **F**raction (EF) is increased from 60% at rest to as much as 90% during heavy exercise, also by the enhanced contractility.
- The decrease in total peripheral resistance as a result of VD in the exercising skeletal muscles, which decreases the after-load, will further augment the SV.
- The increased force of contraction is due to the +ve inotropic effect of:

a) Increased sympathetic activity on the heart:
- It has a +ve inotropic effect (= increasing ventricular contractility, acting on β_1-receptors).

b) Circulating catecholamines:
- Mainly epinephrine hormone.
- They have a +ve inotropic effect (= increasing ventricular contractility, acting on β_1-receptors).

3- <u>*Increased venous return (VR)*</u>:
- Venous return is the most important factor that determines COP. Any increase in VR increases COP and vice versa.
- During muscular exercise, VR is increased due to:

a) Increased sympathetic activity:
- They act on (alpha) α_1-receptors present in the walls of veins to produce venoconstriction.

- Contraction of the walls of veins decreases their capacity leading to increase the pressure inside them to facilitate VR down pressure gradient.

b) Mobilization of blood from viscera:
- Due to both venoconstriction & contraction of abdominal muscles compressing the viscera.

c) Increased thoracic pump activity:
- Increased rate & depth of inspiration associated with muscular exercise lead to:
  - ➢ Increased negativity of intra-thoracic pressure → facilitates VR.
  - ➢ Downward movement of the diaphragm → rises the intra-abdominal pressure & compress abdominal veins.

d) Increased skeletal muscle pump activity:
- Contraction of skeletal muscle during muscular exercise presses the veins from outside squeezing & milking them decreasing their capacity with increased VR.

B) Increased arterial blood pressure:

- Increased ABP during exercise is needed for:
  - ➢ Creation of more force to push blood through the muscle tissue vessels.
  - ➢ Stretching the walls of the vessels.
- Increased ABP during exercise is the result of increased sympathetic activity, through the following effects:

a) Increased pumping activity of the heart:
- Because the sympathetic stimulation increases cardiac contraction (acting on β_1-receptors).
- This leads to increased stroke volume with subsequent elevation of the ABP (mainly **S**ystolic **B**lood **P**ressure, SBP).

b) Increased venous return:
- Caused mainly by venoconstriction (acting on α_1-receptors).
- This leads to increased stroke volume with also elevation of the ABP (mainly SBP).

c) Arteriolar vasoconstriction:
- By acting on α_1-receptors in the arteriolar wall.
- Arteriolar VC increases the peripheral resistance with subsequent elevation of the ABP (mainly **D**iastolic **B**lood **P**ressure, DBP).

C) Re-distribution of blood flow:

- The regional blood flow during exercise will be as follow:

Blood Flow	Level
- Coronary	Increased

- Cerebral	Constant
- Pulmonary	Increased
- Visceral	Decreased
- Skeletal	Increased
- Cutaneous	Decreased (Temperature ☹?)
- Renal	Decreased

II) Local Changes in the Active Muscle:

A) Increased muscle blood flow:

- The skeletal muscle blood flow is increased (as mentioned before) through :
  - Mainly by local metabolic mechanism (= release of VD metabolites); e.g., adenosine, K^+, CO_2, H^+.
  - Sympathetic cholinergic fibers (from cerebral cortex, only at the start of exercise).
  - Circulating catecholamines (mainly epinephrine) acting on β_2-adrenergic receptors.
  - Increased temperature within the working muscle also leads to arteriolar VD.

B) Capillary dilatation:

- During exercise, all capillaries of the active muscle are opened & dilated in addition to dilatation of the already opened capillaries.
- These capillary changes are essential for effective exchange between blood and muscle fibers supplying them with their requirements.

C) Increased lymph flow:

- The increase in lymph flow is essential to prevent accumulation of excessive tissue fluid with the development of edema.
- During exercise, lymph flow is increased by:
  - Increased thoracic pump activity provides suction force that help in lymph drainage.
  - Activity of skeletal muscles provides a massaging action help in lymph drainage.
  - Arterial pulsation provides a pumping action that compress nearby lymphatic vessels helping in drainage.

D) Increased oxygen uptake:

- The rate of oxygen uptake by the active muscle is enhanced because of:
  - Increased muscle blood flow with increased availability of oxygen.
  - Shift of oxygen–hemoglobin dissociation curve to the right.

Adaptation to Exercise Training
(Cardiovascular Adaptation)

A) Cardiac output:

- Both at rest & at any given level of exercise, trained athletes have a larger stroke volume & lower heart rate than un-trained individuals. This called "Cardiac Conditioning".
- Exercise training leads to:
  1- *Increase the resting stoke volume due to*:
    - Increase in ventricular volume.
    - Increase in ventricular wall thickness.

  2- *Decrease the resting heart rate due to*:
    - Increase vagal tone.

B) Cardiac hypertrophy:

- As in marathon runner.
- It is due to increase synthesis of proteins → ↑ the size of individual cardiac muscle fiber → ↑ thickness of ventricular wall → ↑ force of ventricular contraction → more powerful ejection during systole.

C) Cardiac reserve:

- Cardiac reserve is the difference between maximal cardiac output & the resting basal cardiac output.
- e.g., In marathon runner:

  Cardiac reserve = COP (maximal) – COP (resting)
  = 35 L/min – 5 L/min
  = 30 L/min

- Cardiac reserve is increased by:
  - Short term mechanism (= controlling SV & HR).
  - Long term mechanism (= dilatation & hypertrophy)
- But remember cardiac reserve has a limit (☹?).

D) Coronary blood vessels:

- Exercise training leads to changes in the coronary vascular bed, including:
  - Increases the density of coronary arterioles and capillaries.
  - Increases the production of nitric oxide for promoting VD.
  - Decreases the compression of the coronary vessels in systole, due to the lower cardiac rate (and thus frequency of systoles) in trained athletes.

E) Cardiac vascular diseases:

- Exercise training greatly reduces cardiovascular disease, with the decrease in incidence and severity of myocardial infarction.